

CSP #710B

Normative Aging Study

The Normative Aging Study is a longitudinal study of aging in men, established by the VA in 1961. To provide an initially healthy population, over 6000 male volunteers from the greater Boston area were screened; men were disqualified from participation in the study if they had a history of conditions such as heart disease, cancer, gout, diabetes, peptic ulcer, recurrent asthma, or high blood pressure. With these criteria, 2280 men were accepted into the NAS, ranging from 21-81 years old. Participants were enrolled and received their first medical examinations between 1961-1970.

Oral Health of Ambulatory Care Patients

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Abstract: This project assessed the clinical oral health status of VA patients and examined the relationship between oral health and both sociodemographic factors and dental care utilization. Data were collected on 538 users of VA ambulatory medical care. Oral health was assessed by clinical examinations, and dental use and sociodemographic information are based on self-report. Younger, more educated VA patients with higher incomes had more teeth, fewer untreated and treated root caries,

and were less likely to be edentulous or to have dentures. Dental utilization emerged as the most important aspect of veterans' oral health status, even after sociodemographic factors were controlled. Compared with the general population, veterans have poorer oral health with the exception of coronal caries. The importance of sociodemographic factors and dental utilization that has been found in other studies applies to veterans' oral health as well.

(Mil Med 166:171-178, 2001)
MAVERIC Boston, MA

Hostility and the Metabolic Syndrome in Older Males: The Normative Aging Study

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Abstract: Several studies have shown that hostility, as measured by the Minnesota Multiphasic Personality Inventory-derived Cook-Medley Hostility Scale (Ho), is positively associated with several cardiovascular risk factors, possibly accounting for the relationship between Ho scores and cardiovascular mortality. This study was undertaken to examine associations between hostility and cardiovascular risk factors representing the metabolic syndrome in 1081 older men who participated in the Normative Aging Study. Subjects included men who completed the Minnesota Multiphasic Personality Inventory in 1986 and who participated in a subsequent laboratory examination within 1 to 4 years. Total and subscale Ho scores were computed, and associations with anthropometric data, cigarette smoking, dietary information, serum lipids, blood pressure, and fasting glucose and insulin levels were examined. The total Ho score was

positively associated with waist/hip ratio, body mass index, total caloric intake, fasting insulin level, and serum triglycerides. The Ho score was inversely related to education and high-density lipoprotein cholesterol concentration. Path analysis also suggested that the effects of hostility on insulin, triglycerides, and high-density lipoprotein cholesterol were mediated by its effects on body mass index and waist/hip ratio which, in turn, exerted their effects on lipids and blood pressure through insulin. The results are consistent with those of prior research and also suggest that, in older men, hostility may be associated with a pattern of obesity, central adiposity, and insulin resistance, which can exert effects on blood pressure and serum lipids. Furthermore, effects of hostility on the metabolic syndrome appear to be mediated by body mass index and waist/hip ratio.

(Psychosomatic Research 62:7-16, 2000)
MAVERIC Boston, MA

Optimism and Depression as Predictors of Physical and Mental Health Functioning: The Normative Aging Study

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Abstract: Dispositional optimism has been linked in previous studies to better health outcomes. We sought to examine the independent associations of dispositional optimism and depressive symptoms with physical and mental functioning in a cohort of healthy middle-aged and older men. The study was conducted among 659 subjects in the VA Normative Aging Study. Dispositional optimism and depressive symptomatology were measured in 1991 and 1990, respectively, by the Life Orientation Test and the Center for Epidemiologic Studies – Depression Scale (CES-D). The dependent variables, functioning and well-being, were measured in 1992 by the Medical

Outcomes Study Short-Form Health Survey (SF-36). In multivariate regression models, optimism was associated with higher levels of general health perceptions, vitality, and mental health, and lower levels of bodily pain, but not to physical functioning, social functioning, or role limitations due to physical or emotional problems. Depressive symptomatology was associated with reduced levels of functioning across all SF-36 domains. The findings for optimism and depression were statistically significant after mutual adjustment in multivariate regression models. Optimism and depression are independent predictors of functional status among aging men.

(Ann Behav Med 22(2):127-130, 2000)
MAVERIC Boston, MA

Negative Affectivity and Health-related Quality of Life

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Abstract: Although personality is known to influence patients' self-ratings of health, its effects on reports of health-related quality of life (HRQOL) have not been fully described. We examined the relationship between a dimension of personality called negative affectivity (NA; a general disposition to experience negative mood states) and HRQOL, controlling for age and common chronic physical and mental diseases.

We used data from 3 samples of veterans: the VA Normative Aging Study, The Veterans Health Study, and the VA Women's Health Project. For each of the 8 SF-36 scales and the physical and mental component summary scales, 2 regression models were estimated, the first of which included only chronic diseases and age and the second of which add NA.

NA was consistently negatively associated with SF-36 scale scores in

bivariate analyses. The regression models indicated that across the 3 samples, NA explained between 0% and 13.9% additional variance in the scales, with the least additional variance in the physical function domains (range 0-2.6%) and the most in the mental function domains (range 0-13.9%). Results from the summary scales were similar: NA explained none of the variance in the physical component summary and 3.5% to 10.4% in the mental component summary. These results were largely consistent across the 3 samples.

These results suggest the importance of NA in patients' rating of HRQOL. Thus, clinicians and researchers who rely on measures such as the SF-36 to assess health status should consider that personality, as well as underlying health, can affect self-ratings of HRQOL.

(Med Care 38(8):858-867, 2000)
MAVERIC Boston, MA

Relations between Health-related Quality of Life and Well-being: The Gerontologist's New Clothes?

AVRON SPIRO III PHD, RAYMOND BOSSE' PHD

Abstract: Is the recent construct of health-related quality of life (HQL) distinct from what gerontologists have long referred to as "well-being" or "life satisfaction"? We addressed this question using data from men in the VA Normative Aging Study to examine relations among 12 scales assessing HQL and 7 scales of well-being (WB). We hypothesized that these two constructs would be distinct factorially, and that the derived factors would have different correlates. Correlations between scales of HQL and WB were moderate. When the 19 scales were factored, four factors were extracted with HQL and WB scales generally loading on separate factors. The factors had distinct patterns of relations with

general quality of life, personality, and the presence of a health problem, controlling for sociodemographics. These results suggest that HQL is distinct from the older construct of well-being. Although the two constructs are conceptually related, there is only a moderate amount of statistical overlap between them. Gerontologists should readily adopt health-related quality of life, which maintains continuity with such classics as well-being. This new construct, although needing slight alterations to broaden its assessment of well-being and life satisfaction, holds promise as more than an accessory in the study of health and well-being among older persons.

(Int J Aging Hum Dev 50(4):287-318, 2000)
MAVERIC Boston, MA

Self-reported and Clinical Oral Health in Users of VA Health Care

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Abstract: This article describes the oral health of users of Veterans Administration (VA) health care using both clinical and self-report measures, and models relationships between these measures and self-perceived oral health. We conducted a cross-sectional study of 538 male users of VA outpatient care in the Boston area. Questionnaires assessed self-reported oral health, oral-specific health-related quality of life, health behaviors, and sociodemographic information. Clinical data were collected on oral mucosa status, number of teeth and root tips, dental caries, and periodontal treatment need. We report clinical and self-reported oral health status by age group (era of military service). We regressed models of self-perceived oral health on clinical indices and self-reported measures of the impact of oral health on daily life, adjusting for socio-demographic characteristics and health behavior.

Among the participants age 65-91 years old, 2.8%, 18.7%, and 41.5% rated their oral health as excellent, very good, or good, respectively. Among 50-64 year-old men, the corresponding values were 1.4%, 18.5% and 40.4%, while among those aged 22 to 49 years old, the values were 2.3%, 17% and 34.1%. Tooth loss was common among users of VA care; 34% of those aged 65-90 years, 28% of those aged 50-64 years, and 8% of those aged 25-49 years had no teeth. Periodontal treatment needs were uniformly high among persons with teeth; mild mucosal change was common, and 10% had root tips. Regression models showed self-perceived oral health was better in persons with more teeth and recent dental treatment, and worse with tooth mobility, coronal decay, and more medical problems. Measures of the impact of oral conditions on daily life added significantly to the amount of explained variance in self-perceived oral health.

(J Geron MedSci 56A(1):M55-M62, 2001)
MAVERIC Boston, MA

Physician-diagnosed Medical Disorders in Relation to PTSD Symptoms in Older Male Military Veterans

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Abstract: The association between physician-diagnosed medical disorders and combat-related posttraumatic stress disorder (PTSD) symptoms was examined in 605 male combat veterans of World War II and the Korean conflict. Physician exams were performed at periodic intervals beginning in the 1960s. PTSD symptoms were assessed in 1990. Cox regression was used to examine the onset of each of 12 disorder categories as a function of PTSD symptoms, controlling for age,

smoking, alcohol use, and body weight at study entry. Even with control for these factors, PTSD symptoms were associated with increased onset of arterial, lower gastrointestinal, dermatologic, and musculoskeletal disorders. There was only weak evidence that PTSD mediated the effects of combat exposure on morbidity. Possible mediators of the relationship between combat exposure, PTSD, and physical morbidity are discussed.

(Health Psych 19(1):91-97, 2000)
MAVERIC Boston, MA

Personality, Family History, and Alcohol Use among Older Men: The VA Normative Aging Study

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Abstract: We examined personality traits (Sociability, Impulsivity, Neuroticism) as mediators of the effects of family history on alcohol outcomes.

A sample of 485 men reported on family history of alcohol problems in 1973, completed the Eysenck Personality Inventory in 1976, and responded to a survey on alcohol use in 1982.

Using structural equation modeling, family history was found to have direct

effects on drinks per day and on the number of alcohol problems, as well as indirect effects mediated through Neuroticism. There were no effects of Sociability or Impulsivity on either alcohol outcome.

In this sample of older men, family history had both direct and indirect effects, and personality traits found to affect alcohol outcomes were different from those that have been found in younger men.

(Alcoholism: Clinical and Experimental Research 24: 501-511, 2000)
MAVERIC Boston, MA

Predictors of Continued Smoking Over 25 Years of Follow-up in the Normative Aging Study

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Abstract: This study tested the hypothesis that a high daily consumption of cigarettes and addiction to smoking are risk factors for long-term continuation of smoking. Longitudinal data from 986 men in the VA Normative Aging Study cohort identified as smokers at baseline were entered into a survival analysis encompassing 25 years of follow-up. Key variables were age, cigarettes/day, education, and

psychological addiction. Results showed that younger men and heavier smokers were more likely to remain smokers long-term. Education and addiction were not significant predictors of continued smoking in this analysis. Findings support the need for smoking cessation interventions to be applied as early as possible following initiation of smoking, particularly for heavy smokers.

(American Journal of Public Health 90:404-406, 2000)
MAVERIC Boston, MA

Change and Stability in Personality: A 5-year Study of the MMPI-2 in Older Men

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RAYMOND BOSSE' PHD

Abstract: Although widely used, the MMPI is seldom examined longitudinally in studies of normal populations. We conducted a 5-year longitudinal study of the MMPI-2 on a community sample of older men, analyzing change at both the aggregate and the individual level. In 1986 and 1991, 1,072 participants of the Normative Aging Study (mean age = 61) completed the MMPI-2.

Although significant mean change was observed for 16 of 35 validity, clinical, supplementary, and content scales, few exceeded 1 T-score point. Test-retest correlations ranged from 0.55 to 0.85, indicating moderate stability. Analyses at the individual level revealed greater change; for example,

on each scale, some men changed as much as 20 to 40 points.

The distribution of scores for each scale was divided at the clinical cutoffs, allowing comparison of an individual's placement over time. While most men remained stable in the normal range on any given scale, 4% to 20% changed placement. Across the scales as a group, the typical man changed more than 10 points on 5 scales. In the aggregate, there was high stability of MMPI-2 scores over 5 years. Despite the relatively high differential and absolute stability characterizing the sample as a whole, examination of change at the individual level revealed that a much greater extent of change was observed for some persons.

(Basic Sources on the MMPI-2, James N. Butcher Ed, Minneapolis MN: University of Minnesota Press, pp. 443-462, 2000)
MAVERIC Boston, MA

**Maximal and Partial Expiratory Flow Rates in a Population
Sample of 10- To 11-Yr-Old Schoolchildren.
Effect of Volume History and Relation
to Asthma and Maternal Smoking**

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Abstract: The effect of volume history on forced expiratory flow rates has been reported to differ between patients with asthma and healthy persons, and it has been hypothesized that the peripheral airway inflammation of patients with asthma may underlie this difference. There are no published data, however, on the distribution of such volume history effects or the relation of these effects to airways disease in children. We obtained combined partial and maximal forced expiratory flow-volume curves on 1,834 children, age 10-11 yr, in eight communities in the United States and Canada. The effect of a deep inhalation on forced expiratory flow rates at low lung volumes was quantitated by the ratio of V (30) during a maximal expiratory maneuver (V (30M)) to V (30) during a partial expiratory maneuver (V (30P)). The V (30M)/V (30P) ratio was

slightly higher among girls than boys (1.26 versus 1.18, $p = 0.0001$) indicating that a deep inhalation increased V (30) slightly more among girls than among boys. The V (30M)/V (30P) ratio was related to neither history of asthma nor to maternal smoking. In contrast, most spirometric indices from either the maximal or the partial expiratory flow-volume curve were lower in association with a history of asthma or a report of maternal smoking. The ratio of FEF(25-75)/FVC was particularly consistent as a measurement that discriminated both of these effects in boys and girls. These results suggest that the measurement of volume history effects offers no benefits for epidemiological studies of childhood respiratory disease whereas spirometric indices such as the FEV(25-75)/FVC ratio are quite sensitive to the effects of asthma and environmental tobacco smoke exposure on the airways.

(Am J Respir Crit Care Med 162(Pt 1):436-9, 2000)
MAVERIC Boston, MA

Effect of Low Level Lead Exposure on Hyperuricemia and Gout Among Middle Aged and Elderly Men: The Normative Aging Study

NA Shadick MD, R Kim MD, S Weiss MD, MH Liang MD, D Sparrow Dsc, H Hu MD

Abstract: *Objective:* To determine whether longterm lead accumulation is associated with hyperuricemia and gouty arthritis among middle aged and elderly men. *METHODS:* In a retrospective cohort study, 777 male participants were evaluated between August 1991 and October 1996 in the Department of Veterans Affairs Normative Aging Study, a 35 year longitudinal study of aging. We examined the development of gout and an increased uric acid level in relation to lead, adjusting for other known risk factors. Lead levels were measured in blood and by K x-ray fluorescence (K-XRF) technique in tibial (cortical) and patellar (trabecular) bone. *RESULTS:* Blood lead levels in this mostly Caucasian (97%) population were low (mean 5.9 microg/dl, SD 3.5). In a

multivariate analysis adjusting for the risk factors, age, body mass index, diastolic blood pressure, alcohol intake, and serum creatinine level, there was a positive association between patellar bone lead and uric acid levels ($p = 0.02$). Of 777 participants, 52 (6.7%) had developed gouty arthritis. In logistic regression of similar covariates, body mass index ($p < 0.0001$) and serum creatinine level ($p = 0.005$) were the strongest determinants of gout; neither bone nor blood lead levels predicted gout in this cohort. *CONCLUSION:* The longterm accumulation of lead is associated with an increased uric acid level in middle aged and elderly men. However, this study shows no association between lead and gouty arthritis at the levels arising from community exposure.

(*J Rheumatol* 27(7):1708-12, 2000)
MAVERIC Boston, MA

Bone Lead and Blood Lead Levels in Relation to Baseline Blood Pressure and the Prospective Development of Hypertension

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Abstract: Between 1991 and 1997, the authors studied 833 participants of the Normative Aging Study in a substudy of bone lead levels (measured by K-shell x-ray fluorescence), blood lead levels, and hypertension. Among these subjects, 337 were classified as normotensive, and 182 and 314 were classified as having borderline and definite hypertension, respectively, at baseline. Among the 519 subjects with no history of definite hypertension at baseline, cross-sectional analyses revealed positive associations between systolic blood pressure and bone lead levels. Of the 474 subjects who were free from definite hypertension at baseline and had follow-up data, 74 new cases of definite hypertension were

reported. Baseline bone lead levels were positively associated with incidence of hypertension. In proportional hazards models that controlled for age, age squared, body mass index, and family history of hypertension, an increase in patella (trabecular) lead from the midpoint of the lowest quintile to that of the highest quintile was associated with a rate ratio of definite hypertension of 1.71 (95% confidence interval: 1.08, 2.70). No association was found with blood lead level. These results support the hypothesis that cumulative exposure to lead, even at low levels sustained by the general population, may increase the risk for hypertension.

(Am J Epidemiol 153:164-71, 2001)
MAVERIC Boston, MA

97-010

Seattle ERIC

All patients with bacterial infection in their bloodstream were followed in time to determine the predictors of long-term survival after this infection, and also to describe the types of bacteria that cause these infections. A total of 404 cases of this infection in 322 persons occurred between 1994-1997 at one VA Medical Center. The most frequently identified source of the infection was an intravenous line. The poorest survival occurred in veterans with infections of the blood caused by fungus. Persons at the time of the infection who were in shock, admitted to an intensive care unit, ill with another serious medical condition, or had expressed the wish to not be resuscitated in the event of cardiac arrest also had a poorer survival. Many such infections are potentially preventable, and this study helped to identify the settings where such preventive efforts may have the most benefit.

Four Year Prospective Evaluation of Nosocomial Bacteremia: Epidemiology, Microbiology, and Patient Outcome

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Abstract: A prospective study of all patients with clinically significant nosocomial bacteremia at one institution from 1994 to 1997 was performed to: (1) describe the epidemiology and microbiology of nosocomial bacteremias; (2) determine the crude mortality associated with such infections; and (3) identify independent predictors of mortality. Four hundred four episodes of bacteremia occurred in 322 patients; the crude in-hospital mortality was 31%. Coagulase-negative staphylococci, *Staphylococcus aureus*, and enterococci were the leading pathogens, and intravascular catheters were the most

frequently identified source. The highest mortality occurred in patients with candidemia (67%). Independent predictors of mortality included evidence of shock at the time of infection, acquisition of bacteremia in an intensive care unit, a "Do Not Attempt Resuscitation" order, and the presence of certain comorbid conditions (e.g., malignancy, HIV infection). Because many of these infections may be preventable, education of health care providers and strict adherence to established infection control practices are critical.

(Diagnostic Microbiology & Infectious Disease 38(3):131-40, 2000)
ERIC Seattle, WA

CSP #027

18-F-Fluorodeoxyglucose (FDG) Positron Emission Tomography (PET) Imaging in Patients with Solitary Pulmonary Nodules

This economic substudy is using meta-analysis and medical decision models to study the cost-effectiveness of Positron Emission Tomography for diagnosis of solitary pulmonary nodules (SPN) and for cancer staging in patients with non-small cell lung cancer (NSCLC). We performed a meta-analysis that identified 37 studies of FDG-PET for diagnosis of pulmonary nodules and larger pulmonary mass lesions. However, only six studies limited enrollment to participants with pulmonary nodules. Seven additional studies provided separate results for participants with pulmonary nodules. The studies enrolled a total of 450 participants with pulmonary nodules. Study methodological quality was fair, although sample sizes were small and blinding was often incomplete. We combined studies with meta-analytic statistical method. The median specificity of this test was 83.3% accuracy; at this level of accuracy, the test was 94.2% sensitive.

Accuracy of Positron Emission Tomography for Diagnosis of Pulmonary Nodules and Mass Lesions: A Meta-analysis

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Abstract: *Objective:* To estimate the diagnostic accuracy of FDG-PET for malignant focal pulmonary lesions.

Data Sources: Studies published between January 1966 and September 2000 in the MEDLINE and CANCERLIT databases; reference lists of identified studies; abstracts from recent conference proceedings; and direct contact with investigators.

Study Selection: Studies that examined FDG-PET or FDG with a modified gamma camera in coincidence mode for diagnosis of focal pulmonary lesions; enrolled at least 10 participants with pulmonary nodules or masses, including at least 5 participants with malignant lesions; and presented sufficient data to permit calculation of sensitivity and specificity were included in the analysis.

Data Extraction: Two reviewers independently assessed study quality and abstracted data regarding prevalence of malignancy and sensitivity and specificity of the imaging test. Disagreements were resolved by discussion.

Data Synthesis: We used a meta-analytic method to construct summary receiver operating characteristic curves. Forty studies met inclusion criteria. Study methodological quality was fair. Sample sizes were small, and blinding was often incomplete. For 1474 focal pulmonary lesions of any size, the maximum joint sensitivity and specificity (the upper left point on the receiver operating characteristic curve at which sensitivity and specificity are equal) of FDG-PET was 91.2% (95% confidence

interval, 89.1%-92.9%). In current practice, FDG-PET operates at a point on the summary receiver operating characteristic curve that corresponds approximately to a sensitivity and specificity of 96.8% and 77.8%, respectively. There was no difference in diagnostic accuracy for pulmonary nodules compared with lesions of any size ($P=.43$), for semiquantitative methods of image interpretation compared with qualitative methods

($P=.52$), or for FDG-PET compared with FDG imaging with a modified gamma camera in coincidence mode ($P=.19$).

Conclusions: Positron emission tomography with 18-fluorodeoxyglucose is an accurate noninvasive imaging test for diagnosis of pulmonary nodules and larger mass lesions, although few data exist for nodules smaller than 1 cm in diameter. In current practice, FDG-PET has high sensitivity and intermediate specificity for malignancy.

(*JAMA* 285(7):914-924, 2001)
CSPCC Palo Alto, CA

CSP #380

Prospective Evaluation of Risk Factors for Large (>1 cm) Colonic Adenomas in Asymptomatic Subjects

The risk of colon cancer (the second leading cause of death in North America) increases with age. Panels of medical experts generally agree on the importance of screening average risk individuals over the age of 50 and recommend a variety of screening tests including fecal occult blood tests, sigmoidoscopy (partial examination of the colon), or complete colonoscopy. Although the need for screening is clear, questions remain regarding which individuals are at highest risk, how often they should be screened, and with which type of screening test. This cooperative study was designed to answer these questions by enrolling a large number (over three thousand) of asymptomatic individuals, age 50-75, who provided complete information on all known important risk factors for colon cancer such as smoking, family history, dietary history, etc., and who had a complete colon exam to determine the size and location of adenomatous (pre-cancerous) polyps and/or cancer.

The results showed that advanced disease was present in approximately one out of ten otherwise asymptomatic patients. This reinforces the need for some type of screening in individuals over 50. More importantly, of those patients with advanced disease, approximately one in three would not have been detected if the screening exam had been sigmoidoscopy, i.e., a partial exam. This means that sigmoidoscopy would miss significant numbers of cases of advanced disease. Most of the cases (67%) with advanced disease in the part of the colon not reached by sigmoidoscopy would have been missed. This is important because there is increased risk of advanced disease with age for this part of the colon.

Use of Colonoscopy to Screen Asymptomatic Adults for Colorectal Cancer

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Abstract: *Background and Methods:* The role of colonoscopy in screening for colorectal cancer is uncertain. At 13 Veterans Affairs medical centers, we performed colonoscopy to determine the prevalence and location of advanced colonic neoplasms and the risk of advanced proximal neoplasia in asymptomatic patients (age range, 50 to 75 years) with or without distal neoplasia. Advanced colonic neoplasia

was defined as an adenoma that was 10 mm or more in diameter, a villous adenoma, an adenoma with high-grade dysplasia, or invasive cancer. In patients with more than one neoplastic lesion, classification was based on the most advanced lesion.

Results: Of 17,732 patients screened for enrollment, 3196 were enrolled; 3121 of the enrolled patients (97.7 percent) underwent complete examination of the

colon. The mean age of the patients was 62.9 years, and 96.8 percent were men. Colonoscopic examination showed one or more neoplastic lesions in 37.5 percent of the patients, an adenoma with a diameter of at least 10 mm or a villous adenoma in 7.9 percent, an adenoma with high-grade dysplasia in 1.6 percent, and invasive cancer in 1.0 percent. Of the 1765 patients with no polyps in the portion of the colon that was distal to the splenic flexure, 48 (2.7 percent) had advanced proximal neoplasms. Patients with large adenomas (>10 mm) or small adenomas

(<10 mm) in the distal colon were more likely to have advanced proximal neoplasia than were patients with no distal adenomas (odds ratios, 3.4 [95 percent confidence interval, 1.8 to 6.5] and 2.6 [95 percent confidence interval, 1.7 to 4.1], respectively). However, 52 percent of the 128 patients with advanced proximal neoplasia had no distal adenomas.

Conclusion: Colonoscopic screening can detect advanced colonic neoplasms in asymptomatic adults. Many of these neoplasms would not be detected with sigmoidoscopy.

(*N Engl J Med* 343:162-168, 2000)
CSPCC Perry Point, MD

The VA HDL Intervention Trial (HIT): Secondary Prevention of Coronary Heart Disease in Men With Low HDL-Cholesterol and Desirable LDL-Cholesterol

Recent findings in the VA-HIT study show that for patients with coronary heart disease (CHD) an increase in their good cholesterol or HDL-C cholesterol (high density lipoprotein cholesterol) is associated with a reduction in further CHD events, including heart attacks and death from heart disease. Gemfibrozil, the drug tested, resulted in decreases in triglycerides, but these did not lead to decreases in coronary events. Reductions in the bad cholesterol or LDL-C cholesterol (low density lipoprotein cholesterol) also did not reduce the number of heart attacks or coronary deaths.

VA-HIT was undertaken in 2531 men with known heart disease and low HDL-C. Gemfibrozil significantly reduced coronary heart disease events by 22% compared to placebo.

Relation of Gemfibrozil Treatment and Lipid Levels with Major Coronary Events VA-HIT: A Randomized Controlled Trial

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FOR THE VA-HIT STUDY GROUP

Abstract: Context: A low plasma level of high-density lipoprotein cholesterol (HDL-C) is a major risk factor for coronary heart disease (CHD). A secondary prevention study, the Veterans Affairs High-Density Lipoprotein Intervention Trial (VA-HIT), demonstrated that CHD events were significantly reduced during a median follow-up of 5.1 years by treating patients with the fibric acid derivative gemfibrozil when the predominant lipid abnormality was low HDL-C.

Objective: To determine if the reduction in major CHD events with gemfibrozil in VA-HIT could be attributed to changes in major plasma lipid levels.

Design: Multicenter, randomized, double-blind, placebo-controlled trial conducted from September 1991 to

August 1998.

Setting: The Department of Veterans Affairs Cooperative Studies Program, in which 20 VA medical centers were participating sites.

Participants: A total of 2531 men with a history of CHD who had low HDL-C levels (mean, 32 mg/dL [0.83 mmol/L]) and low low-density lipoprotein cholesterol (LDL-C) levels (mean, 111 mg/dL [2.88 mmol/L]).

Intervention: Participants were randomly assigned to receive gemfibrozil, 1200 mg/d (n=1264), or matching placebo (n=1267).

Main Outcome Measure: Relation of lipid levels at baseline and averaged during the first 18 months of gemfibrozil treatment with the combined incidence of nonfatal myocardial

infarction and CHD death.

Results: Concentrations of HDL-C were inversely related to CHD events. Multivariable Cox proportional hazards analysis showed that CHD events were reduced by 11% with gemfibrozil for every 5-mg/dL (0.13-mmol/L) increase in HDL-C ($P=.02$). Events were reduced even further with gemfibrozil beyond that explained by increases in HDL-C values, particularly in the second through fourth quintiles of HDL-C values during treatment. During gemfibrozil

treatment, only the increase in HDL-C significantly predicted a lower risk of CHD events; by multivariable analysis, neither triglyceride nor LDL-C levels at baseline or during the trial predicted CHD events.

Conclusions: Concentrations of HDL-C achieved with gemfibrozil treatment predicted a significant reduction in CHD events in patients with low HDL-C levels. However, the change in HDL-C levels only partially explained the beneficial effect of gemfibrozil.

(*JAMA* 285(12):1585-1591, 2001)
CSPCC West Haven, CT

CSP #995

Trial to Evaluate the Effect of Digitalis on Mortality in Heart Failure (VA-NHLBI)

The incidence, preventive factors, morbidity, and mortality associated with the development of supraventricular tachyarrhythmias (SVTs) in patients with congestive heart failure (CHF) are poorly defined. In the Digitalis Investigation Group trial, patients with CHF who were in sinus rhythm were randomly assigned to digoxin (n=3889) or placebo (n=3899) and followed up for a mean of 37 months. In CHF patients in sinus rhythm, it was found that older age, male sex, longer duration of CHF, and increased cardiothoracic ratio predicted an increased risk for experiencing SVT. Development of SVT is a strong independent predictor of mortality, stroke, and hospitalization for CHF in this population. Prevention of SVT may prolong survival and reduce morbidity in CHF patients.

Incidence, Predictive Factors, and Prognostic Significance of Supraventricular Tachyarrhythmias in Congestive Heart Failure

JAMES MATHEW MBBS FCCP, SALLY HUNSBERGER PHD, JEROME FLEG MD, FRANCES MCSHERRY MS,
WILLIAM WILLIFORD PHD, AND SALIM YUSEF DPHIL FOR THE DIGITALIS INVESTIGATION GROUP

Abstract: *Background:* The incidence, predictive factors, morbidity, and mortality associated with the development of supraventricular tachyarrhythmias (SVTs) in patients with congestive heart failure (CHF) are poorly defined.

Methods: In the Digitalis Investigation Group trial, patients with CHF who were in sinus rhythm were randomly assigned to digoxin (n=3889) or placebo (n=3899) and followed up for a mean of 37 months. Baseline factors that predicted the occurrence of SVT and the effects of SVT on total mortality, stroke, and hospitalization for worsening CHF were determined.

Results: Eight hundred sixty-six patients (11.1%) had SVT during the study period. Older age (odds ratio

(OR), 1.029 for each year increase in age; $p=0.0001$), male sex (OR, 1.270; $p=0.0075$), increasing duration of CHF (OR, 1.003 for each month increase in duration of CHF; $p=0.0021$), and a cardiothoracic ratio of >0.50 (OR, 1.403; $p=0.0001$) predicted an increased risk of experiencing SVT. Left ventricular ejection fraction, New York Heart Association functional class, and treatment with digoxin vs placebo were not related to the occurrence of SVT. After adjustment for other risk factors, development of SVT predicted a greater risk of subsequent total mortality (risk ratio [RR]=2.451; $p=0.0001$), stroke (RR=2.352; $p=0.0001$), and hospitalization for worsening CHF (RR=3.004; $p=0.0001$).

Conclusion: In CHF patients in sinus rhythm, older age, male sex, longer duration of CHF, and increased cardiothoracic ratio predicted an increased risk for experiencing SVT. Development of SVT is a strong

independent predictor of mortality, stroke, and hospitalization for CHF in this population. Prevention of SVT may prolong survival and reduce morbidity in CHF patients.

(Chest 118:914-922, 2000)

CSPCC Perry Point, MD and CSPCRPCC Albuquerque, NM

C.L.E.A.R. (Carotid Lesion Epidemiology and Risk) Study

The paraoxonase protein is involved in heart disease risk. We identified multiple changes in the promoter region of the paraoxonase gene that were associated with changes in the amount of paraoxonase protein. We examined these by multiple methods to isolate their separate effects on the activity of the enzyme.

Effects of 5' Regulatory-Region Polymorphisms on Paraoxonase Gene (PON1) Expression

VH BROPHY, RL JAMPSA, JB CLENDENNING, LA MCKINSTRY, GP JARVIK, CE FURLONG

Abstract: Human HDL-associated paraoxonase (PON1) hydrolyzes a number of toxic organophosphorous compounds and reduces oxidation of LDLs and HDLs. These properties of PON1 account for its ability to protect against pesticide poisonings and atherosclerosis. PON1 also hydrolyzes a number of lactone and cyclic-carbonate drugs. Among individuals in a population, PON1 levels vary widely. We previously identified three polymorphisms in the PON1 regulatory region that affect expression levels in cultured human hepatocytes. In this study, we determined the genotypes of three regulatory-region polymorphisms for 376 white individuals and examined their effect on plasma-PON1 levels, determined by rates of phenylacetate hydrolysis. The -108 polymorphism had a significant effect on PON1-activity level, whereas the -162 polymorphism had a lesser effect. The -909 polymorphism, which is in linkage disequilibrium with the other sites,

appears to have little or no independent effect on PON1-activity level in vivo. Other studies have found that the L55M polymorphism in the PON1-coding region is associated with differences in both PON1-mRNA and PON1-activity levels. The results presented here indicate that the L55M effect of lowered activity is not due to the amino acid change but is, rather, largely due to linkage disequilibrium with the -108 regulatory-region polymorphism. The codon 55 polymorphism marginally appeared to account for 15.3% of the variance in PON1 activity, but this dropped to 5% after adjustments for the effects of the -108 and Q192R polymorphisms were made. The -108C/T polymorphism accounted for 22.8% of the observed variability in PON1-expression levels, which was much greater than that attributable to the other PON1 polymorphisms. We also identified four sequence differences in the 3' UTR of the PON1 mRNA.

(*AM J Hum Genet* 68(6):1428-1436, 2001)
ERIC Seattle, WA

Seattle ERIC

Epidemiologic and health services research often rely upon computerized databases to assess patient outcomes. One of these outcomes is the death of a patient. Unfortunately, not all deaths are recorded in the computerized databases used for research. Therefore, the purpose of this study was to determine the extent to which Department of Veterans Affairs database information about the vital status of veterans agrees with Washington State death certificates. Using data from the VA database, vital status was determined for 19,481 Washington State resident veterans hospitalized in Washington VA hospitals from 1994 to 1997, and for 33,602 Washington State resident veterans who were seen as outpatients during 1997. The agreement on vital status between VA and Washington State records was excellent for hospitalized veterans. 3108 individuals (86.2% of all deaths) appeared in both files. Of those deaths missing in the VA files, 71% had no service-connected disability or VA pension or other compensation. Among outpatients, agreement between the death files was very good. 372 individuals (69.8% of all deaths) appeared in both files. Of those deaths missing in the VA files, 63% had no service-connected disability or VA pension or other compensation. Therefore, VA death files are a valid source of vital status information for veterans hospitalized in recent years. However, for veterans having exclusively outpatient visits, the VA files miss a substantial proportion of deaths. For these patients, alternative means of vital status determination are warranted.

Assessment of vital status in Department of Veterans Affairs national databases: comparison with state death certificates

JA DOMINITZ, C MAYNARD, EJ BOYKO

Abstract: *Purpose:* To determine the extent to which Department of Veterans Affairs database vital status information agrees with Washington State death certificates.

Methods: Using each data source, vital status was determined for 19,481 Washington State resident veterans hospitalized in Washington VA hospitals from 1994 to 1997, and for 33,602 Washington State resident veterans who were seen as outpatients during 1997.

Results: The agreement between VA and Washington State records was

excellent for hospitalized veterans ($\kappa=0.91$, $p<0.0001$). 3108 individuals (86.2% of all deaths) appeared in both files. Of those deaths missing in the VA files, 71% had no service-connected disability or VA pension or other compensation. Among outpatients, agreement between the death files was very good ($\kappa=0.82$, $p<0.001$). 372 individuals (69.8% of all deaths) appeared in both files. Of those deaths missing in the VA files, 63% had no service-connected disability or VA pension or other compensation.

Conclusions: The VA death files are a valid source of vital status information for veterans hospitalized in recent years. However, for veterans having exclusively outpatient visits, the VA files

miss a substantial proportion of deaths. For these patients, alternative means of vital status ascertainment are warranted.

(Annals of Epidemiology 11:281-286, 2001)
ERIC Seattle, WA

Osseointegrated Implants for Type II Diabetic Patients

Diabetes is a common disease. People with diabetes tend to have problems with healing that might affect the bonding of dental implants with the lower jawbone. This study examined how well one style of dental implant bonded in the lower jaws of 89 men. Two implants were surgically inserted into the lower jaw of each man and were allowed to heal for about four months. A denture designed to be attached to the two implants was made for each man. Sixteen of the 178 implants failed to successfully bond with the lower jawbone. Implants failed to bond more frequently in men who had been diabetic for a long time. Short implants were more likely to fail than long implants. Although some implants failed to successfully bond with the jawbone, the fact that most of them did supports the use of dental implants for diabetic patients.

Dental Endosseous Implant Assessments in a Type 2 Diabetic Population: A Prospective Study

JOHN W OLSON DDS MS, ALAN F SHERNOFF DDS, JEFFREY L TARLOW DDS,
JOHN A COLWELL MD PHD, JAMES P SCHEETZ PHD, STEPHEN F BINGHAM PHD

Abstract: Diabetes mellitus, a prevalent disorder worldwide, is associated with systemic adverse sequelae, such as wound healing alterations, which may affect osseointegration of dental implants. This prospective multicenter study assessed the success of 2-stage endosseous root-form implants (3 different implant systems) placed in the mandibular symphysis of 89 male type 2 diabetic subjects. The implants were uncovered approximately 4 months after placement, restored with an implant-supported, Hader bar clip-retained overdenture, and maintained at scheduled follow-up data collection examinations for 60 months after loading. Sixteen (9.0%) of the 178 implants failed. Life table methods calculated implant survival at approximately 88%, from prosthesis placement through the 60-month follow-

up, and at approximately 90% from implant placement through the observation period. No implants failed between surgical placement and uncovering, 5 failed at uncovering, 7 failed after uncovering before prosthesis placement, and 4 failed after prosthesis placement. Fasting plasma glucose (FPG) and glycosylated hemoglobin (HbA1c) values were determined before implant placement (baseline) and approximately 4 months later at surgical uncovering (follow-up). The 5-year implant outcomes (successes versus failures) were analyzed against the following predictor variables: (1) baseline and follow-up FPG values, (2) baseline and follow-up HbA1c values, (3) subject age, (4) duration of diabetes (years), (5) baseline diabetic therapy, (6) smoking history, and (7) implant length. Regression analysis found only duration of diabetes ($P<.025$) and

implant length ($P < .001$) to be statistically significant predictors of implant failure. There was no statistically significant difference in failure rates between the 3

different implant systems used. This study supports the use of dental implants in type 2 diabetic patients.

(Int J Oral Maxillofac Implants 15:811-818, 2000)
CSPCC Perry Point, MD

The Pharmacoeconomics of Buprenorphine Treatment of Opiate Dependence

A detailed analysis of clinical trials that compared buprenorphine to methadone for the treatment of opiate dependence disorders found that buprenorphine was more effective than low doses of methadone, but slightly less effective than the recommended dose of methadone. Although this difference is statistically significant, it is small compared to the wide variance in outcomes of different methadone treatment programs.

A Meta-Analysis Comparing Buprenorphine to Methadone for Treatment of Opiate Dependence

PG Barnett PhD, JH Rodgers MS, DA Bloch PhD

Abstract: *Background:* The unique pharmacologic properties of buprenorphine may make it a useful maintenance therapy for opiate addiction. This meta-analysis considers the effectiveness of buprenorphine relative to methadone.

Methods: A systematic literature search identified five randomized clinical trials comparing buprenorphine to methadone. Data from these trials were obtained. Retention in treatment was analyzed with a Cox proportional hazards regression. Urinalyses for opiates were studied with analysis of variance and a common method of handling missing values. A meta-analysis was used to combine these results.

Results: Subjects who received 8-12 mg/day buprenorphine had 1.26 times the relative risk of discontinuing treatment (95% confidence interval of

1.01-1.57) and 8.3% more positive urinalyses (95% confidence interval of 2.7% to 14%) than subjects receiving 50-80 mg/day methadone. Buprenorphine was more effective than 20-35 mg/day methadone. There was substantial variation in outcomes in the different trials.

Conclusions: The variation between trials may be due to differences in dose levels, patient exclusion criteria, and provision of psychosocial treatment. The difference in the effectiveness of buprenorphine and methadone may be statistically significant, but the differences are small compared to the wide variance in outcomes achieved in different methadone treatment programs. Further research is needed to determine if buprenorphine treatment is more effective than methadone in particular settings or in particular subgroups of patients.

(Addiction 96:683-690, 2001)
CSPCC Palo Alto, CA

CSP #277A

A Follow-Up Study of the Medical and Surgical Therapies for Gastroesophageal Reflux Disease Trial

A follow-up study was conducted from October 1997 through October 1999 of a prospective randomized trial (CSP #277) of medical and surgical antireflux treatments in patients with complicated GERD. Mean (median) duration of follow-up was 10.6 years (7.3 years) for medical patients and 9.1 years (6.3 years) for surgical patients. Two hundred thirty-nine (97%) of the original 247 study patients were found (79 were confirmed dead). Among the 160 survivors (157 men and 3 women; mean [SD] age, 67 [12] years), 129 (91 in the medical treatment group and 38 in the surgical treatment group) participated in the follow-up.

Survival during a period of 140 months was decreased significantly in the surgical vs the medical treatment group largely because of excess deaths from heart disease. Patients with Barrett esophagus at baseline developed esophageal adenocarcinomas at an annual rate of 0.4%, whereas these cancers developed in patients without Barrett esophagus at an annual rate of only 0.07%. There was no significant difference between groups in incidence of esophageal cancer. This study suggests that antireflux surgery should not be advised with the expectation that patients with GERD will no longer need to take antisecretory medications or that the procedure will prevent esophageal cancer among those with GERD and Barrett esophagus.

Therapies for Gastroesophageal Reflux Disease

STUART JOHN SPECHLER MD, EDWARD LEE MD, DENNIS AHNEN MD, RAJ K GOYAL MD, IKUO HIRANO MD, FRANCISCO RAMIREZ MD, JEAN-PIERRE RAUFMAN MD, RICHARD SAMPLINER MD, THOMAS SCHNELL MD, STEPHEN SONTAG MD, Z RENO VLAHCEVIC MD, RENEE YOUNG MD, WILLIAM WILLIFORD PhD

Abstract: *Context:* Severe gastro-esophageal reflux disease (GERD) is a lifelong problem that can be complicated by peptic esophageal stricture and adenocarcinoma of the esophagus.

Objective: To determine the long-term outcome of medical and surgical therapies for GERD.

Design and Setting: Follow-up study conducted from October 1997 through October 1999 of a prospective randomized trial of medical and surgical antireflux treatments in patients with

complicated GERD. Mean (median) duration of follow-up was 10.6 years (7.3 years) for medical patients and 9.1 years (6.3 years) for surgical patients.

Participants: Two hundred thirty-nine (97%) of the original 247 study patients were found (79 were confirmed dead). Among the 160 survivors (157 men and 3 women; mean [SD] age, 67 [12] years), 129 (91 in the medical treatment group and 38 in the surgical treatment group) participated in the follow-up.

Main Outcome Measures: Use of anti-reflux medication, Gastroesophageal Reflux Disease Activity Index (GRACI) scores, grade of esophagitis, frequency of treatment of esophageal stricture, frequency of subsequent antireflux operations, 36-item Short Form health survey (SF-36) scores, satisfaction with antireflux therapy, survival, and incidence of esophageal adenocarcinoma, compared between the medical antireflux therapy group and the fundoplication surgery group. Information on cause of death was obtained from autopsy results, hospital records, and death certificate.

Results: Eighty-three (92%) of 90 medical patients and 23 (62%) of 37 surgical patients reported that they used antireflux medications regularly ($P<.001$). During a 1-week period after discontinuation of medication, mean (SD) GRACI symptom scores were significantly lower in the surgical treatment group (82.6 [17.5] vs 96.7 [21.4] in the medical treatment group; $P=.003$). However, no significant differences between the group were found in grade of esophagitis, frequency

of treatment of esophageal stricture and subsequent antireflux operations, SF-36 standardized physical and mental component scale scores, and overall satisfaction with antireflux therapy. Survival during a period of 140 months was decreased significantly in the surgical vs the medical treatment group (relative risk of death in the medical group, 1.57; 95% confidence interval, 1.01-2.46; $P=.047$), largely because of excess deaths from heart disease. Patients with Barrett esophagus at baseline developed esophageal adenocarcinomas at an annual rate of 0.4%, whereas these cancers developed in patients without Barrett esophagus at an annual rate of only 0.07%. There was no significant difference between groups in incidence of esophageal cancer.

Conclusion: This study suggests that antireflux surgery should not be advised with the expectation that patients with GERD will no longer need to take antisecretory medications or that the procedure will prevent esophageal cancer among those with GERD and Barrett esophagus.

(JAMA 285(18):2331-2338, 2001)
CSPCC Perry Point, MD

CSP #470

A Randomized, Multi-center, Controlled Trial of Multi-Modal Therapy in Gulf War Illnesses

In May of 1999 the VA launched a study to try to determine if adding cognitive behavioral therapy, aerobic exercise, or the combination of the two on top of usual and customary care will help improve the quality of life of veterans suffering from Gulf War Veteran's Illnesses. The study will take place over a two and a half-year period and enroll more than one thousand veterans from 18 VA and two Department of Defense medical centers.

A Multicenter Two by Two Factorial Trial of Cognitive Behavioral Therapy and Aerobic Exercise for Gulf War Veterans' Illnesses: Design of a Veterans Affairs Cooperative Study (CSP #470)

PETER GUARINO MPH, PETER PEDUZZI PHD, SAM T DONTA MD, CHARLES C ENGEL JR MD MPH, DANIEL J CLAUW MD, DAVID A WILLIAMS PHD, JAMES S SKINNER PHD, ANDRE BARKHUIZEN MD, LEWIS E KAZIS PHD, AND JOHN R FEUSSNER MD FOR THE CSP #470 STUDY GROUP

Abstract: The Department of Veterans Affairs (VA) Cooperative Studies Program (CSP) Study #470 is a 2x2 factorial trial designed to evaluate the hypothesis that both cognitive behavioral therapy (CBT) and aerobic exercise will significantly improve physical function in participants with Gulf War veterans' illnesses (GWVI), and that adding CBT to aerobic exercise will provide further incremental benefit. One thousand three hundred fifty-six veterans will be randomized to one of four treatment arms: CBT plus aerobic exercise plus usual and customary care, aerobic exercise plus usual and customary care, CBT plus usual and customary care, or usual and customary care alone. The study duration is 2.5 years with 1.5 years of intake and 1 year of follow-up. The primary outcome measure is the proportion of veterans improved more than seven units on the physical component summary (PCS)

scale of the Short Form Health Survey for Veterans (SF-36V) measured 12 months after randomization. This generic quality-of-life measure was chosen because there is no disease-specific measure for GWVI and the symptoms of GWVI span a wide range of physical manifestations that are related to the domains covered by the PCS scale. Sample size was determined to detect all six pairwise comparisons between the four treatment arms with 90% power and a Bonferroni adjustment for an overall type I error of 0.05 or $0.05/6 = 0.0083$. CSP #470 was initiated in May 1999 in 18 VA and two Department of Defense medical centers. To date this represents the largest randomized trial designed to evaluate treatments for individuals with unexplained physical symptoms. This paper will focus on the rationale and unique features of the study design.

(Control Clin Trials 22:310-332, 2001)
CSPCC West Haven, CT

CSP #418

NIDCD/VA Hearing Aid Clinical Trial

More than 14 million people in the U.S. could benefit by using a hearing aid, but only about 5 million have sought help for their problem. There is a scarcity of well-conducted, large scale clinical trials evaluating the effectiveness of hearing aids.

In 1993 the VA and the National Institute on Deafness and Other Communication Disorders formed a partnership to conduct such trials. CSP #418 is the first clinical trial conducted from that partnership. It compared the effectiveness of three commonly used hearing aid designs, known as peak clipping, linear amplification with compression limiting, and wide dynamic range compression.

Efficacy of 3 Commonly Used Hearing Aid Circuits: A Crossover Trial

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Abstract: *Context:* Numerous studies have demonstrated that hearing aids provide significant benefit for a wide range of sensorineural hearing loss, but no carefully controlled, multicenter clinical trials comparing hearing aid efficacy have been conducted.

Objective: To compare the benefits provided to patients with sensorineural hearing loss by 3 commonly used hearing aid circuits.

Design: Double-blind, 3-period, 3-treatment crossover trial conducted from May 1996 to February 1998.

Setting: Eight audiology laboratories at Department of Veterans Affairs medical centers across the United States.

Patients: A sample of 360 patients with bilateral sensorineural hearing loss (mean age, 67.2 years; 57% male; 78.6% white).

Intervention: Patients were randomly assigned to 1 of 6 sequences of linear peak clipper (PC), compression limiter

(CL), and wide dynamic range compressor (WDRC) hearing aid circuits. All patients wore each of the 3 hearing aids, which were installed in identical casements, for 3 months.

Main Outcome Measures: Results of tests of speech recognition, sound quality, and subjective hearing aid benefit, administered at baseline and after each 3-month intervention with and without a hearing aid. At the end of the experiment, patients ranked the 3 hearing aid circuits.

Results: Each circuit markedly improved speech recognition, with greater improvement observed for soft and conversationally loud speech (all 52-dB and 62dB conditions, $P \leq .001$). All 3 circuits significantly reduced the frequency of problems encountered in verbal communication. Some test results suggested that CL and WDRC circuits provided a significantly better listening experience than PC circuits in

word recognition ($P = .002$), loudness ($P = .003$), overall liking ($P = .001$), aversiveness of environmental sounds ($P = .02$), and distortion ($P = .02$). In the rank-order ratings, patients preferred the CL hearing aid circuits more frequently (41.6%) than the WDRC (29.8%) and the PC (28.6%) ($P = .001$ for CL vs both WDRC and PC).

(*JAMA* 284(14):1806-1813, 2000)
CSPCC Hines, IL

Conclusions: Each circuit provided significant benefit in quiet and noisy listening situations. The CL and WDRC circuits appeared to provide superior benefits compared with the PC, although the differences between them were much less than the differences between the aided vs unaided conditions.

CSP #706D

HIV Seroprevalence and Risks in Veterans with Severe Mental Illness

The HIV Seroprevalence and Risks in Veterans with Severe Mental Illness (SMI) study is a four-year longitudinal study of veterans with severe mental illness. This Durham ERIC study supplements a collaborative study funded by the National Institute of Mental Health. The Durham VA is the only VA site represented in the study and is collaborating with four non-VA sites. The objective of the study is to determine the prevalence of HIV and other related infections such as Hepatitis C, along with associated risk behaviors in veterans with SMI. SMI diagnoses include schizophrenia, schizoaffective disorder, bipolar disorder, and posttraumatic stress disorder (PTSD). HIV risk behaviors include injection drug use and sexual promiscuity, personal and social-contextual factors, and comorbid mental disorders. Study participation consists of a one-hour structured HIV-risk behavior interview and a blood and urine sample.

The two articles described below present preliminary results of the study and evaluation of a physical and mental health survey in a sample of people with SMI.

Prevalence of HIV, Hepatitis B, and Hepatitis C in People with Severe Mental Illness

STANLEY ROSENBERG PHD, LISA GOODMAN PHD, FRED OSHER MD, MARVIN SWARTZ MD,
SUSAN ESSOCK PHD, MARIAN BUTTERFIELD MD MPH, NIEL CONSTANTINE PHD,
GEORGE WOLFORD PHD, MICHELE SALYERS PHD

Abstract: This study assessed seroprevalence rates of HIV, hepatitis B virus (HBV), and hepatitis C virus (HCV) among individuals with severe mental illness (SMI).

Participants (n=931) were patients undergoing inpatient or outpatient treatment in Connecticut, Maryland, New Hampshire, or North Carolina.

The prevalence of HIV infection in this sample (3.1%) was approximately 8 times the estimated US population rate but lower than rates reported in previous studies of people with SMI.

Prevalence rates of HBV (23.4%) and HCV (19.6%) were approximately 5 and 11 times the overall estimated population rates for these infections, respectively.

Elevated rates of HIV, HBV, and HCV were found. Of particular concern are the high rates of HCV infection, which are frequently undetected. Individuals with HCV infection commonly fail to receive appropriate treatment to limit liver damage and unknowingly may be a source of infection to others.

(Am J Public Health 91:31-37,2001)
ERIC Durham, NC

Reliability and Validity of the SF-12 Health Survey Among People With Severe Mental Illness

MICHELLE SALYERS PHD, HAYDEN BOSWORTH PHD, JEFFREY SWANSON PHD,
JERILYNN LAMB-PAGONE RN MSN CS, FRED OSHER MD

Abstract: The objective of this work was to assess the reliability and validity of the Medical Outcomes Study Short-Form 12-Item Health Survey (SF-12) in a large sample of people with severe mental illness (SMI).

We examined the internal factor structure of the SF-12, compared component scores for this sample with normative levels, examined test-retest reliability, and examined convergent and divergent validity by comparing SF-12

scores to other indexes of physical and mental health.

The SF-12 distinguished this sample of people with SMI from the general population, was stable over a 1-week interval, consisted of 2 fairly distinct factors, and was related to physical and mental health indexes in expected ways.

The SF-12 appears to be a psychometrically sound instrument for measuring health-related quality of life for people with SMI.

(Med Care 38:1141-1150,2000)
ERIC Durham, NC

CSP #290

Monotherapy of Hypertension

This study compared six different blood pressure lowering drugs and placebo to determine their individual effectiveness if each were administered as single-drug treatment for hypertension. The initial results published in 1993 (N. Engl. J. Med. 328:914-21, 1993), showed that patient characteristics such as age and race were strong predictors of which drug would be most successful. Patients who were unresponsive to the first drug were randomized to a second single-drug therapy. The results of this phase showed that switching to a second drug is as effective as the common practice of adding a second drug to the initial therapy. Patients who did not respond to the second drug received a combination of the two drugs. The results demonstrated that a combination of drugs, which were not successful when used individually, had a high probability of success in controlling blood pressure, particularly when the combination included a diuretic.

The two articles below report additional results from the study. The first article is a book chapter reporting on the design and outcomes of the trial. The other article examines the effects of the drugs on plasma lipids and lipoprotein profiles.

Department of Veterans Affairs Cooperative Study on Monotherapy of Hypertension

BARRY J MATERSON, DOMENIC J REDA

Abstract: Dr. Edward D. Freis assembled the first major Veterans Administration (VA) Cooperative Study Group on Antihypertensive Agents. He is renowned for proving that oral drug treatment of hypertension conferred a major benefit by reducing the damaging impact of hypertension on target organs. When that study was planned in 1960, the prevailing wisdom was that "benign essential" hypertension should not be treated at all! Dr. Freis subsequently organized and conducted a series of cooperative studies that made significant contributions to our understanding of hypertension and its therapy. The studies were always organized to provide information to practicing physicians in their care of hypertensive patients. Most of the study groups involved seven VA centers with

two seven-center groups operating simultaneously on different projects.

The Department of Veterans Affairs Cooperative Study Group on Antihypertensive Agents (participants are listed in Section XIII) started planning for its largest cooperative study in September 1984. Fourteen (later 15) VA medical centers would follow the same protocol with the intention to enroll 1400 patients. It required more than 2 years for the approval process, funding, training, drug acquisition, and packaging and shipping of drugs and study forms to the 14 original participating VA medical centers. Patient intake began on October 10, 1986, and the first patient was randomized to the Titration Phase on November 19, 1986. A fifteenth medical center (Dallas) joined the group two weeks later. The study

progressed relatively smoothly, although multiple site visits, special trouble shooting, and additional training sessions were required. Annual study group meetings were of considerable value in maintaining the integrity of the study. The progress of the study was continuously monitored by an internal executive committee, and external data monitoring board that had the power to recommend to the chief of the program that the study be stopped if necessary, and the central human rights committee. The patient intake period ended on September 30, 1989, and the last patient completed follow-up on September 30, 1990. The first major manuscript was published in the New England Journal of Medicine on April 1,

1993. An additional 16 manuscripts based on this data set have been published and at least three more are pending.

The primary objective of this study was to determine the blood pressure lowering efficacy, ability to maintain blood pressure control, and incidence of medical terminations of different classes of antihypertensive agents used as single-drug therapy (monotherapy). The six drug classes (and representative drug) selected were: α -adrenergic blocking agents (atenolol), angiotensin converting enzyme inhibitors (captopril), central α_2 -agonists (clonidine), calcium antagonists (diltiazem-SR), thiazide diuretics (hydrochlorothiazide), and peripheral α_1 -blocking agents (prazosin).

*(Black, HR. Clinical Trials in Hypertension, Chapter 13:283-311, 2001 New York: Marcel Dekker, Inc.)
CSPCC Hines, IL and CSPCRPCC Albuquerque, NM*

Are the Lipid Effects of Antihypertensive Agents Serious?

M RAJ LAKSHMAN PHD, DOMENIC J REDA MS, BARRY J MATERSON MD, WILLIAM C CUSHMAN MD,
EDWARD D FREIS MD FOR THE DEPARTMENT OF VETERANS AFFAIRS
COOPERATIVE STUDY GROUP ON ANTIHYPERTENSIVE AGENTS

Abstract: Since many antihypertensive drugs adversely affect plasma lipids and lipoprotein profiles, we compared the long-term effects of six agents on plasma lipids in 1,292 hypertensive men. Patients achieving diastolic blood pressure control with hydrochlorothiazide showed no adverse changes in

plasma lipids, whereas nonresponders exhibited increases in triglycerides, total cholesterol, and low-density lipoprotein cholesterol. Changes in plasma lipids among treatment groups after 1 year were nonsignificant. We conclude that the six agents tested may therefore be safely prescribed.

*(Cardiology Review 17(3):38-42, 2000)
CSPCC Hines, IL and CSPCRPCC Albuquerque, NM*

CSP #712B

Psychological Adaptation of U.S. Military Peacekeepers

This is a series of studies designed to evaluate mental health in US military peacekeepers. Three cohorts of peacekeepers are being examined: Veterans of the Somalia, Bosnia, and Kosovo missions. In the Bosnia and Kosovo studies, baseline mental health status was evaluated before soldiers deployed to the missions. The mental health outcomes evaluated include: (a) PTSD prevalence, and PTSD symptom severity, (b) depression problems, and (c) anger and hostility problems. We are also examining the multivariate predictors of the three mental health outcomes. The predictors studied include: Demographic and military service characteristics, the frequency of exposure to Potentially Traumatizing Events (PTE), peacekeeping and peace-enforcement stressors (e.g., boredom, chronic threat, being the victim of harassment and taunting), pre-deployment psychopathology, prior exposure to stressful overseas missions, and pre-deployment exposure to PTE. We are also examining barriers to care in this new class of veterans.

The Psychological Impact of Military Peacekeepers

BRETT LITZ PHD, ELISA BOLTON PHD

Abstract: This article first provides an overview of how peacekeeping missions have changed since the inception of the United Nations. It then provides a summary of the stressors associated with peacekeeping from the perspective of four different peacekeeping missions that roughly represent

a continuum of peacekeeping stress. It then summarizes the unique stressors of peacekeeping and the psychological impact of these missions. It concludes with suggestions about ways of improving the psychological health of future peacekeepers.

(Encyclopedia of Stress Ed. G. Fink. Academic Press, San Diego, CA: 134-137, 2000)
MAVERIC Boston, MA

Report of Prior Exposure to Potentially Traumatic Events and PTSD in Troops Poised for Deployment

ELISA BOLTON PHD, BRETT LITZ PHD, THOMAS BRITT PHD, LIZABETH ROEMER PHD

Abstract: Exposure to potentially traumatic events (PTEs), PTSD symptomatology, and the mental health status of 2,947 military personnel were assessed prior to deployment on a peacekeeping mission. Approximately 74% of the soldiers reported being exposed to at least one PTE. The mean number of PTEs reported was 2.38, most of which did not occur during previous deployments. Approximately 6 percent of the participants exceeded our

screening criteria for PTSD and 43% of the participants endorsed elevated levels of psychological distress. These findings document a high rate of exposure to PTEs in soldiers prior to their deployment. These results also highlight the need to screen for PTEs when attempting to isolate the rates of PTSD following a specific traumatic event and to examine the effects of cumulative exposure to PTEs.

(Journal of Traumatic Stress 14:249-256, 2001)
MAVERIC Boston, MA

CSP #420

Group Treatment of Posttraumatic Stress Disorder

This paper presents and describes the study design for CSP #420.

Design of Department of Veterans Affairs Cooperative Study No. 420: Group Treatment of Posttraumatic Stress Disorder

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AND FRANK Y HSIEH PHD

Abstract: Posttraumatic stress disorder (PTSD) is a significant problem for a large number of veterans who receive treatment from the Department of Veterans Affairs (VA) health care system. VA Cooperative Study 420 is a randomized clinical trial of group psychotherapy for treating PTSD among veterans who sought VA care. Participants (n = 360) at ten sites were randomly assigned to receive one of the two treatments: active treatment that embedded exposure therapy in a group context, or comparison treatment that avoided trauma focus and instead addressed current interpersonal problems. Treatment was delivered weekly to groups of six participants for 30 weeks, followed by five monthly booster sessions. Follow-up assessments were conducted at the end

of treatment (7 months) and the end of boosters (12 months) for all participants. Long-term follow-up data were collected for a subset of participants at 18 and 24 months. The primary outcome is PTSD severity; other symptoms, functional status, quality of life, physical health, and service utilization also were assessed. Data analysis will account for the clustering introduced by the group nature of the intervention. The pivotal comparison was at the end of treatment. Analyses of subsequent outcomes will concentrate on the question of the durability of effects. The study provides an example of how to address the unique challenges posed by multisite trials of group psychotherapy through attention to methodological and statistical issues. This article discusses these challenges and describes the design and methods of the study.

(Control Clin Trials 22:74-88, 2001)
CSPCC Palo Alto, CA

CSP #3

A Multi-site Randomized Trial of Team Managed Home Based Primary Care

The purpose of this study was to determine whether total health care costs and hospital costs for severely disabled and terminally ill veterans can be reduced through a program of team-managed home-based primary care (TM/HBPC) compared to customary care. Patient functional outcomes and patient and caregiver quality of life and satisfaction were also compared.

The article below reports on the primary outcomes of the study. The terminally ill patients and their caregivers experienced large improvements in their quality of life with the TM/HBPC. Furthermore, the severely disabled patients realized large improvements in satisfaction with their health care. Their caregivers also experienced significant improvements in their quality of life and caregiver burden. The costs of TM/HBPC were 6.8% higher than customary care after 6 months and 12.1% higher after one year.

Effectiveness of Team-Managed Home-Based Primary Care: A Randomized Multicenter Trial

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Abstract: *Context:* Although home-based health care has grown over the past decade, its effectiveness remains controversial. A prior trial of Veterans Affairs (VA) Team-Managed Home-Based Primary Care (TM/HBPC) found favorable outcomes, but the replicability of the model and generalizability of the findings are unknown.

Objectives: To assess the impact of TM/HBPC on functional status, health-related quality of life (HR-QoL), satisfaction with care, and cost of care.

Design and Setting: Multisite randomized controlled trial conducted from October 1994 to September 1998 in 16 VA medical centers with HBPC programs.

Participants: A total of 1966 patients with a mean age of 70 years who had 2

or more activities of daily living impairments or a terminal illness, congestive heart failure (CHF), or chronic obstructive pulmonary disease (COPD).

Intervention: Home-based primary care (n=981), including a primary care manager, 24-hour contact for patients, prior approval of hospital readmissions, and HBPC team participation in discharge planning, vs customary VA and private sector care (n=985).

Main Outcome Measures: Patient functional status, patient and caregiver HR-QoL and satisfaction, caregiver burden, hospital readmissions, and costs over 12 months.

Results: Functional status as assessed by the Barthel Index did not differ for terminal ($P=.40$) or nonterminal (those

with severe disability or who had CHF or COPD) ($P=.17$) patients by treatment group. Significant improvements were seen in terminal TM/HBPC patients in HR-QoL scales of emotional role function, social function, bodily pain, mental health, vitality, and general health. Team-Managed HBPC nonterminal patients had significant increases of 5 to 10 points in 5 of 6 satisfaction with care scales. The caregivers of terminal patients in the TM/HBPC group improved significantly in HR-QoL measures except for vitality and general health. Caregivers of nonterminal patients improved significantly in QoL measures and reported reduced caregiver burden ($P=.008$). Team-Managed HBPC patients with severe disability experienced a 22% relative decrease

(0.7 readmissions/patient for TM/HBPC group vs 0.9 readmissions/patient for control group) in hospital readmissions ($P=.03$) at 6 months that was not sustained at 12 months. Total mean per person costs were 6.8% higher in the TM/HBPC group at 6 months (\$19190 vs \$17971) and 12.1% higher at 12 months (\$31401 vs \$28008).

Conclusions: The TM/HBPC intervention improved most HR-QoL measures among terminally ill patients and satisfaction among non-terminally ill patients. It improved caregiver HR-QoL, satisfaction with care, and caregiver burden and reduced hospital readmissions at 6 months, but it did not substitute for other forms of care. The higher costs of TM/HBPC should be weighed against these benefits.

(JAMA 284:2877-2885, 2000)
CSPCC Hines, IL

CSP #8

Can the Provision of Primary Care Reduce Hospital Readmissions?

This study was designed to test the hypothesis that readmissions may be preventable, using an intervention of providing rapid access to high quality primary care to patients discharged from the hospital. The study found that the intervention actually increased hospital readmissions.

The primary results were published in the May 30, 1996 issue of New England Journal of Medicine. The article below reports on a substudy using the database looking at predictors of non-elective hospital readmissions.

Predicting Non-elective Hospital Readmissions: A Multi-site Study

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Abstract: *Objective:* To determine clinical and patient-centered factors predicting non-elective hospital readmissions.

Design: Secondary analysis from a randomized clinical trial.

Clinical Setting: Nine VA medical centers.

Participants: Patients discharged from the medical service with diabetes mellitus, congestive heart failure, and/or chronic obstructive pulmonary disease (COPD).

Main Outcome Measurement: Non-elective readmission within 90 days.

Results: Of 1378 patients discharged, 23.3% were readmitted. After controlling for hospital and intervention

status, risk of readmission was increased if the patient had more hospitalizations and emergency room visits in the prior 6 months, higher blood urea nitrogen, lower mental health function, a diagnosis of COPD, and increased satisfaction with access to emergency care assessed on the index hospitalization.

Conclusions: Both clinical and patient-centered factors identifiable at discharge are related to non-elective readmission. These factors identify high-risk patients and provide guidance for future interventions. The relationship of patient satisfaction measures to readmission deserves further study.

(*Journal of Clinical Epidemiology* 53:1113-1118, 2000)
CSPCC Hines, IL

CSP #717B

A Prospective Study of Respiratory Function and Illness in Chronic Spinal Cord Injury

Subjects were recruited from a community-based mail survey of 1147 subjects with SCI, and from subjects injured >1 year who received their annual physical at the VA Boston Healthcare System. Subjects underwent measurement of FVC, FEV₁, TLC and subdivisions, maximal inspiratory and expiratory pressures (MIP/MEP), and completed a health questionnaire based on the ATS DLD-78 respiratory questionnaire. A cross-sectional cohort of 360 subjects with chronic SCI was tested from 10/94-8/98.

Predictors of Loud Snoring in Spinal Cord Injury

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Abstract: Predictors of loud snoring were examined in a cohort of 197 subjects with chronic spinal cord injury (SCI) recruited by advertisement and from a Veterans Affairs Medical Center SCI Service. Data were collected on age, marital status, antispasticity medications, duration of injury, level and completeness of injury, stature, and weight. Body mass index (BMI) was calculated for all participants. A health questionnaire was used to collect data on snoring and respiratory history. Habitual snorers were defined as those who reported loud snoring \geq one night/week. The mean age (\pm SD) was 51.2 \pm 14.8 years, and 84 of 197 (42.6%) were habitual snorers. The most obese research subjects, regardless of antispasticity medication use, were more likely to report snoring, but the risk of snoring was greatest among subjects who were obese and used antispasticity

medication. Subjects who used antispasticity medication and had a BMI at or above the median (\geq 25.3) had a 7-fold risk of reporting snoring compared to subjects below the median and who did not use antispasticity medication ($p=0.001$). The greatest risk occurred in those who used diazepam alone or baclofen and diazepam together had a BMI at or above the median. Subjects who used these medications and had a BMI below the median did not have a significantly increased risk. Neurological motor completeness, level of injury, age, and years since injury were not significant predictors of snoring. Because snoring is a marker for obstructive sleep apnea (OSA), the data suggest that in obese individuals with SCI, the use of antispasticity medications may be a risk factor for OSA.

(J Spinal Cord Med 24:30-34, 2001)
MAVERIC Boston, MA

The National VA Surgical Quality Improvement Program (NSQIP)

The NSQIP collects data on patient risk factors, intra-operative variables, and postoperative outcomes on patients undergoing major surgical operations in the VA system. The data are used to monitor the outcomes and performance of the surgical services in the VA. The VA is the first health care system in the U.S. to collect and report such data for surgical services as a whole. The database is also available for VA investigators to conduct research on surgical outcomes. The articles that follow report on the use of the NSQIP as a quality improvement tool and a substudy investigating the comparison of radical and partial nephrectomy in the NSQIP database.

Risk-Adjusted Surgical Outcomes

JENNIFER DALEY, WILLIAM G HENDERSON, AND SHUKRI F KHURI

Abstract: Measures of risk-adjusted outcome are particularly suited for the assessment of the quality of surgical care. The reliability of measures of quality that use surgical outcomes is enhanced by prospective data acquisition and should be adjusted for the preoperative severity of illness. Such measures should be based only on reliable and validated data, and they should apply state-of-the-art analytical methods. The risk-adjusted postoperative mortality rate is useful as a quality measure only in specialties and operations expected to have a high rate

of postoperative deaths. Risk-adjusted complications are more common but are limited as a comparative measure of quality by a lack of uniform definitions and data collection mechanisms. In specialties in which the expected postoperative mortality is low, risk-adjusted functional outcomes are promising measures for the assessment of the quality of surgical care. Measures of cost and patient satisfaction should also be incorporated in systems designed to measure the quality and cost-effectiveness of surgical care.

(Caskey, CT, Austin, C, and Hoxie, J. *Annual Review of Medicine: Selected Topics in the Clinical Sciences* 52:275-287, 2001)
CSPCC Hines, IL

Comparison of Complications after Radical and Partial Nephrectomy: Results from the National Veterans Administration Surgical Quality Improvement Program

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Abstract: *Objective:* To determine whether radical nephrectomy causes less morbidity, less mortality and is associated with a shorter hospital stay than is partial nephrectomy.

Patients and Methods: A total of 1885 nephrectomies (1373 radical and 512 partial) conducted between 1991 and 1998 in the Department of Veterans Affairs (VA) National Surgical Quality Improvement Program were evaluated. Using multivariate analyses, outcomes were risk-adjusted based on 45 preoperative variables to compare mortality and morbidity rates.

Results: The unadjusted 30-day mortality was 2.0% for radical and 1.6% for partial nephrectomy ($P = 0.58$). Risk-adjusting the two groups did not

result in a statistically significant difference in mortality. The 30-day overall morbidity rate was 15% for radical and 16.2% for partial nephrectomy ($P = 0.52$); risk-adjusted morbidity rates were not statistically different. There were no statistically significant differences in the rates of postoperative progressive renal failure, acute renal failure, urinary tract infection, prolonged ileus, transfusion requirement, deep wound infection, or extended length of stay.

Conclusions: Partial nephrectomy carried out in the VA program has low morbidity and mortality rates, comparable with the complication rates after radical nephrectomy.

(*British Journal of Urology International* 86:782-789, 2000)
CSPCC Hines, IL

CSP #141

Comparative Efficacy of Vascular Bypass Materials in Lower Extremity Revascularization

Several different prosthetic materials are available for bypassing areas of occlusion of arteries leading to the legs. This study evaluated, using a prospective comparative protocol, different prostheses to determine which one was the best and offered the best chance of preserving the limbs of veteran patients. The study results will enable vascular surgeons to make an informed choice of a bypass graft material based on knowledge of its comparative efficacy.

A comparative evaluation of polytetrafluoroethylene, umbilical vein, and saphenous vein bypass grafts for femoral-popliteal above-knee revascularization: A prospective randomized Department of Veterans Affairs cooperative study

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DEPARTMENT OF VETERANS AFFAIRS COOP STUDY 141

Abstract: *Purpose:* Currently the choice of a vascular prosthesis for a femoral-popliteal above-knee arterial bypass graft is left to the surgeon's preference, because the available information on comparative evaluations is inconclusive. The Department of Veterans Affairs (VA) Cooperative Study #141 was established to identify whether improved patency exists with different bypass graft materials for patients with femoral-popliteal above-knee bypass grafts.

Methods: Between June 1983 and June 1988, 752 patients at 20 VA medical centers were randomized to receive either an externally supported polytetrafluoroethylene (PTFE; N = 265), human umbilical vein (HUV; N = 261), or saphenous vein (SV; N = 226) for an above-knee femoral-popliteal bypass graft. The indication for the bypass grafting operation was limb salvage in

67.5% of the patients. Patients were observed every 3 months for the first year and every 6 months thereafter. All patients were instructed to take aspirin (650 mg) daily for the duration of the study.

Doppler-derived ankle-brachial indices (ABIs) were determined preoperatively and serially postoperatively. A bypass graft was considered to be patent when the Doppler-derived postoperative ABI remained significantly improved (more than 0.15 units higher than their preoperative value) and additional objective information, such as angiograms or operations, did not contradict these observations. Patency failure also included bypass grafts that were removed because of an infection or aneurysmal degeneration. Patency rates were compared by using the Kaplan-Meier life table analysis.

Results: The cumulative assisted primary patency rates were statistically similar among the different conduit types at 2 years (SV, 81%; HUV, 70%; PTFE, 69%). After 5 years, above-knee SV bypass grafts had a significantly ($P \leq .01$) better patency rate (73%) than HUV bypass grafts (53%), which had a significantly ($P \leq .01$) better patency rate than PTFE bypass grafts (39%). Limb salvage was slightly worse with PTFE conduits.

(*J Vasc Surg* 32:268-277, 2000)
CSPCC Palo Alto, CA

The number of bypass graft thromboses and major amputations within the first 30 days was highest in the HUV group.

Conclusion: The overall results of this prospective randomized study suggest that the SV should be considered as the bypass graft of choice for femoral-popliteal above-knee reconstruction and that, when a prosthetic bypass graft is used, an HUV should also be considered as an alternative choice to PTFE.

CSP #993

Vietnam Era Twin Registry

The Vietnam Era Twin Registry (VETR) consists of 7,375 male-male identical and fraternal twin pairs who served in the military during the Vietnam War. The Registry was originally developed to study the effects of Agent Orange and the long-term health effects for military service in Vietnam. In 1988, the Registry was opened to other VA and non-VA investigators for studying the relative contributions of genetics and the environment to health and disease. The Registry was maintained at the Hines VA Cooperative Studies Program Coordinating Center from 1988 to 2001, and was moved in 2001 to the Seattle Epidemiology Research and Information Center. The two articles below report on two studies using the twin register.

Self-Reported Zygosity and the Equal-Environments Assumption for Psychiatric Disorders in the Vietnam Era Twin Registry

HONG XIAN, JEFFREY F SCHERRER, SETH A EISEN, WILLIAM R TRUE, ANDREW C HEATH, JACK GOLDBERG, MICHAEL J LYONS, AND MING T TSUANG

Abstract: The equal-environments assumption (EEA) in twin studies of psychiatric disorders assumes that the family environment which contributes to risk for a disorder is equally correlated between monozygotic (MZ) and dizygotic (DZ) twin pairs. In a study of psychiatric disorders in female twins, Kendler and colleagues (1993) have demonstrated the utility of a test of the EEA which includes a specified family environmental factor defined by using measures of perceived zygosity. We tested the EEA assumption among 3155 male-male twin pair members of the Vietnam Era Twin Registry for the

following DSM-III-R lifetime disorders: alcohol dependence, marijuana dependence, any illicit drug dependence, nicotine dependence, major depression, and posttraumatic stress disorder. The majority of MZ (81.6%; $n = 1593$) and DZ (90.2%; $n = 1086$) twin pairs agreed with the investigator's assigned zygosity. The best-fitting model for each of these disorders did not allow for a specified family environmental influence. These results support the usefulness of perceived zygosity in tests of the EEA. In male twin pairs, perceived zygosity has little impact on twin similarity for common psychiatric disorders.

(Behavioral Genetics 30(4):303-310, 2000)
CSPCC Hines, IL

Genetic and Environmental Influences on Posttraumatic Stress Disorder, Alcohol and Drug Dependence in Twin Pairs

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JACK GOLDBERG, MING TSUANG, WILLIAM R TRUE

Abstract: We investigated whether and to what degree genetic and environmental contributions overlap among posttraumatic stress disorder (PTSD), alcohol dependence (AD) and drug dependence (DD). Subjects were 3304 monozygotic and dizygotic male-male twin pair members of the Vietnam Era Twin Registry who participated in 1992 telephone administration of the Diagnostic Interview Schedule Version 3 Revised (DIS-3R). Genetic model fitting was performed to estimate the magnitude of genetic and environmental contributions to the lifetime co-occurrence of DSM-III-R PTSD, AD and DD. The liability for PTSD was partially due to a 15.3% genetic contribution

common to AD and DD and 20.0% genetic contribution specific to PTSD. Risk for AD was partially due to a 55.7% genetic contribution common to PTSD and DD. Genetic influences common to PTSD and AD accounted for 25.2% of the total risk for DD. Specific family environmental influence accounted for 33.9% of the total variance in risk for DD. Remaining variance for all three disorders was due to unique environmental factors both common and specific to each phenotype. These results suggest that PTSD, AD and DD each have etiologically distinct components and also have significant genetic and unique environmental contributions in common.

(Drug and Alcohol Dependence 61:95-102, 2000)
CSPCC Hines, IL